Alberta Heritage Foundation
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Decisions on the status of health technologies

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This information paper has been prepared on the basis of available information of which the Foundation is aware from public literature and expert opinion and attempts to be current to the date of publication. It has been externally reviewed. Additional information and comments relative to the information paper are welcome and should be sent to:

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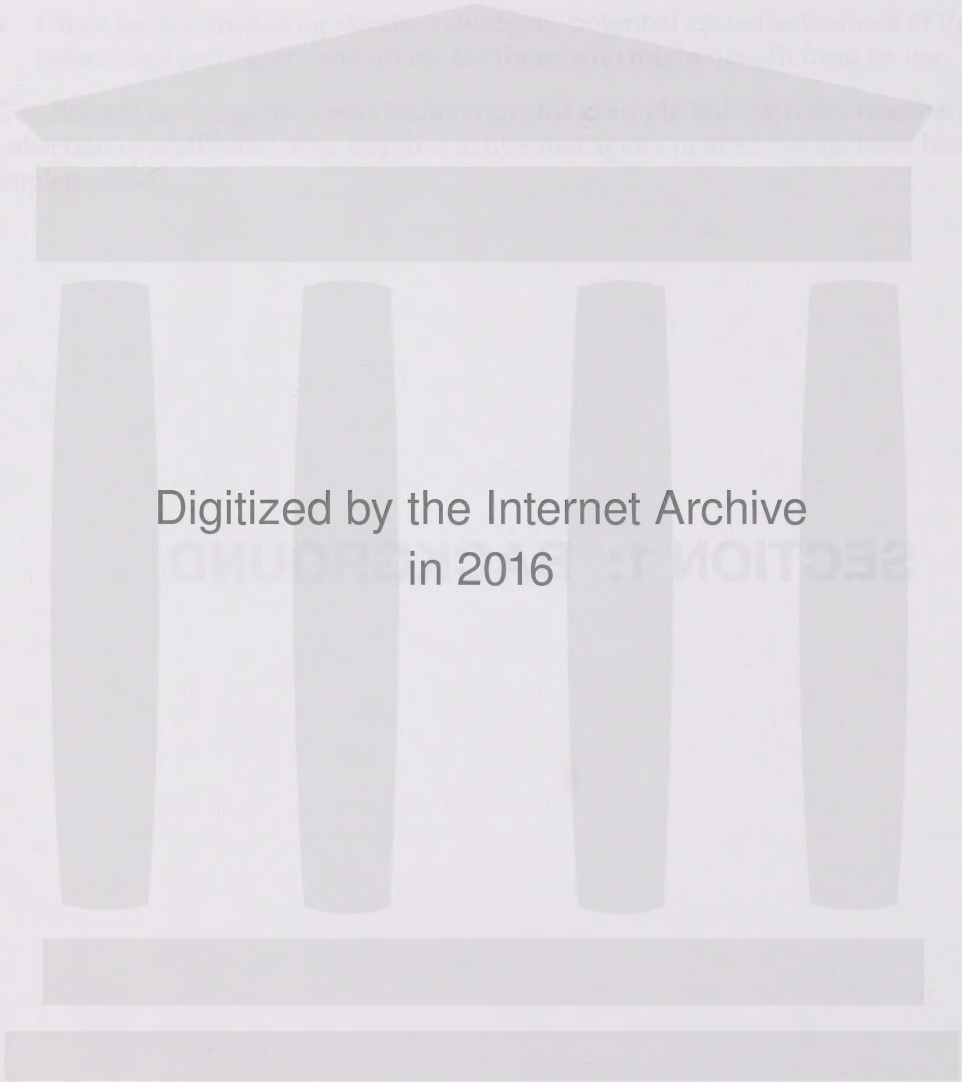
SUMMARY

- This paper is intended to assist health care decision-makers in Alberta in considering when to support the use of emerging health technologies.
- Coverage for a health technology is often denied if it is considered to be 'experimental'. The meaning of 'experimental' in this context is not always entirely clear, though it will be informed by the level of evidence available on the safety and efficacy of a technology.
- Many technologies that can no longer be regarded as experimental, for example some that have been widely used, are still poorly defined in terms of their efficacy or effectiveness. Such technologies may be classified as 'not adequately validated'.
- If the status of an emerging technology has been determined as 'experimental' or 'not adequately validated', further matters need to be considered in making a decision on whether to provide coverage. Health technology assessments indicate that these include the nature of the condition for which the technology is to be used and the availability of effective alternative methods. Opinions from provincial decision-makers suggested that levels of benefit compared to those from alternative interventions and quality of life or functional status of the patient are important considerations.
- Decisions on many emerging technologies will be complex. Availability of relevant data within a realistic time may often present difficulties. There may be a tension between the wish to ensure adequate safety and efficacy and the avoidance of unreasonable delays in the introduction of promising technologies. Approaches which use a combination of different technologies may be particularly difficult to assess.
- In determining whether to provide coverage for an emerging technology, decision-makers should consider:
  - Whether the technology is still experimental (number of persons who have received the intervention, quality of evidence of safety and efficacy, length of follow up).
  - Whether the technology is adequately validated if it is not experimental (quality of evidence of efficacy or effectiveness).
  - Relevance to the local health care system and patient population.

  - Factors that influence HTA recommendations, including the nature of the disease or condition in question, performance and availability of alternative technologies, expected incremental benefit and availability of adequate competency.
  - Other factors, including effects on budgets, potential cost-effectiveness of the technology and equity and access for those who might benefit from its use.

- Conditional coverage for a new technology, for example linking reimbursement to collection of additional data, requires active management after the decision has been implemented.

SECTION 1: BACKGROUND



INTRODUCTION

This paper has been prepared to assist health care decision-makers in Alberta who are responsible for funding the introduction and use of new health technologies. Specifically, it is intended to define the criteria which may be useful in delineating the status of a health technology from a health technology assessor's perspective and from a funder's perspective.

Health technologies of various types, including devices, procedures, information systems and drugs, are continually being developed. As new innovations emerge, authorities are faced with decisions whether to fund them and, if so, to what extent and under what conditions.

Decision-makers will have a number of concerns regarding new technology, which will usually be intended to substitute for or complement existing methods of patient management. Many of these concerns will relate to use of resources – whether support for a new modality is a justifiable use of health care dollars. There will also be a wish, from a public health perspective, to ensure that the technology is safe and effective.

A question that has arisen frequently in Alberta during consideration of applications for funding by the health ministry is whether or not a technology can be regarded as experimental. In the province, if a technology is deemed to be experimental, then there are consequences for how it is regarded in terms of health services supported by the government.

Section 21 of The Alberta Health Care Insurance Act - Alberta Health Care Insurance Regulations states that:

> *"The following are not basic health services or extended health services:*
>
> *(h) services that the Minister, on review of the evidence, determines not to be health services because the services*
>
> *(i) are not required, or*
>
> *(ii) are experimental or applied research."*

However, the meanings of 'experimental' and 'applied research' in this context are not entirely clear. A difficulty that arises here is that 'experimental' is being used, at least in part, with reference to the extent to which a technology has diffused. 'Experimental' does not necessarily mean that an experiment, in the sense of one or more clinical trials, is in progress. This point is even more apparent when consideration is given to technologies which have disseminated quite widely, but for which there is still poor evidence of efficacy or effectiveness from an epidemiological perspective, such technologies would be considered as not established. The evidence and the experiment are incomplete.

Also, from the perspective of health technology assessment, there are questions as to whether experimental technologies in some circumstances may appropriately be supported through provision of funding.

Much of the following discussion addresses the perspective of organizations, particularly government agencies, that fund the procurement and use of health technologies. However, the material presented draws on criteria used in health technology assessment, taking account of the various attributes to be considered in evaluating a new technology. In addition, opinions obtained from decision-makers in health authorities and other organizations are included, which did not necessarily correspond to those of government. Legal aspects of coverage decisions are not considered. Publications cited in the paper were identified using the approach outlined in Appendix A.

Relevant papers in the literature are first reviewed. There is then a description of an empirical study undertaken in the province to obtain opinion from decision-makers on how the status of technologies as experimental or non-experimental might be determined. Issues in determining the status of health technologies and whether to support their use are then illustrated through the findings in a number of assessments undertaken by the Alberta Heritage Foundation for Medical Research (AHFMR). Finally, some suggestions are made for possible future directions for consideration of emerging technologies in the context of Alberta health care.

Introduction of Health Technologies

The question of introduction of new health technology has been discussed in terms of the technology diffusion cycle. Banta and Luce [2] give a five-stage classification:

1. Future technology (not yet developed).
2. Emerging technology (prior to adoption).
3. New technology (in the phase of adoption).
4. Accepted technology (in general use).
5. Obsolete technology (should be taken out of use).

Stage 2 may be of interest to decision-makers in terms of forecasting, and in part be covered by the 'early warning' programs for identification of emerging health technologies that have been established in several countries. These include the series of alerts, known as Techscans, that have been prepared by AHFMR and which are available via the Foundation's website (www.ahfmr.ab.ca).

However, there is no major difficulty in the consideration of support through health services funding at the initial development stage or at first human use (corresponding to the start of the diffusion cycle). At this part of the cycle, a

technology would generally be regarded as experimental – there would still be major uncertainties as to how well and how safely it worked, even in the short term. Support for its use would be derived from other sources, such as private sector funding or research and development grants.

More problematic are the shifts from Stage 2 to 3 and from Stage 3 to 4, where there may well be uncertainty as to when the innovation ceases to become experimental and begins to fall into another category. The stages of transition are typically not clear-cut. The status of a health technology ideally evolves over a continuum, with progress beyond the experimental stage being dependent on a number of factors, which include the quality of the evidence on its performance.

Emerging Health Technologies and Support for Their Use

Much of the commentary in this area has come from the United States (US) and has often been concerned with the legal implications of regulatory and coverage decisions, including those made by health maintenance organizations. Only aspects that seem relevant to decision making in Alberta are considered here.

Definitions and terminology

Various shades of meaning have been attached to 'experimental' and other terms used to describe the status of new technology. Several issues relating to the definition of experimental technology in relation to third-party payers were identified some time ago by Newcomer [16]. He noted that the majority of insurers excluded experimental or unapproved therapies from coverage, but used the dictionary for their definitions. Measures such as survival advantage were not used to define experimental treatment in the courts or in public debate. Defining criteria for experimental in a policy document was a possible solution. Criteria could include a minimal number of successfully-treated patients, a threshold for rate of cure or improvement of quality of life or a randomized controlled trial (RCT) that established benefit over conventional therapy. He also pointed out that making decisions on a case by case basis was currently used by most payers, using evaluation of the literature with implicit criteria.

Ramsey and Pauly [17] draw attention to use by fee for service insurers of the categories 'experimental' and 'discretionary'. Examples they cite include coverage of in vitro fertilization (IVF) (regarded as effective but discretionary), bone marrow transplantation for breast cancer (experimental) and certain screening tests (effective but not cost effective). Saver [22] notes that 'experimental' is not well defined as a concept in the context of US courts proceedings, a point also made by Belk [3]. Crane [6] has suggested that the 'experimental' label is applied to dozens of well-accepted treatments and drugs as an excuse not to pay for them.

In discussing a US case, Brushwood [5] suggests that innovative therapy is sometimes incorrectly referred to as experimental; arguing this is a therapy that is not used in the context of an experiment.

Reiser [18] discussed the boundaries between experimental and standard therapy and the influence of this division on policy, payment, and practice. He suggested a new category, crossover therapy, to describe the many therapies that fall in between. Four criteria were formulated to separate these categories:

- the populations and conditions for which use is helpful;
- the expected outcomes of care;
- the skill, personnel, and site requirements and the economic, ethical, and legal understandings essential for use; and
- the level of knowledge needed to certify that prospective users can apply it well.

He then discusses the use of experimental therapy in desperate situations and of standard therapies in new areas.

Level of evidence required

There is general agreement in the literature that decisions on status and coverage of new or emerging health technologies should be informed by good quality evidence of efficacy. Diamond [7] suggests that the coverage decision should embrace a model of evidence-based medicine, defined as the conscientious and judicious use of current best evidence from clinical care research in the management of individual patients and populations. In the context of coverage decisions, an article by Eddy [8] noted that evidence is considered to be sufficient to draw conclusions if it is peer reviewed, is well controlled, directly or indirectly relates the intervention to health outcomes, and is reproducible both within and outside of research settings. Braslow [4] comments that the fact that an older established therapy has little proof of effectiveness is not a valid reason for approving coverage for a new therapy that also lacks such evidence.

A number of reviews have provided classifications of strength of evidence in terms of the design and quality of studies. The earlier classifications developed by the Canadian Task Force on the Periodic Health Examination (CTFPHE) [25] provide an example. Quality of evidence was specified at five levels, ranging from level I evidence from at least one properly randomized controlled trial to three levels referring to studies of weaker design, to level III (opinions of respected authorities). This hierarchy of evidence is priorized according to study design placing those less susceptable to bias and errors of inference first. Based upon the level of evidence, the CTFPHE classifies its recommendations into four categories. The strongest recommendations (A and E) are reserved for preventive interventions whose value is supported or negated by high quality

evidence (Level I). Recommendations B and D are usually associated with fair quality evidence (Level III).

Availability and relevance of evidence

Forrester et al. [9] discuss the current regulatory process used by the US Food and Drug Administration (FDA) and criticise the delay in approval for marketing of new devices. A limitation is seen to be the time required to collect data in RCTs that are mandated prior to device approvals. They make a distinction between drugs and devices, noting that the latter usually evolves rapidly through several versions and that there is also a typical evolution of user skills. They suggested a facilitated approval process for iterative changes to similar devices, implying that more rigorous levels of proof of efficacy through RCTs may be delayed until after marketing approval. Approval would be linked to acknowledgement that the new device approval could be rescinded if data to support its use do not emerge.

Luce and Brown [13] found that in the USA a pervasive problem in gathering information on devices and procedures was the paucity of timely, relevant and credible data. They, too, draw attention to the limited sources of information about incremental improvements and in possible slower adoption of improved technology. Similarly, Saver [22] mentions that many new technologies do not generate primary evaluative data and that few enjoy an uncritical reception before they are introduced into general practice. Consensus about new treatments may have more to do with whether the treatments follow current fashions in medical theory and less to do with how well they work.

Saver [22] suggests that standards of review should reflect realities of publication delays and conflicting medical opinion involving new treatments. The benchmark that a technology be extensively documented in the medical literature to move beyond experimental status should be modified.

The question of level of evidence needed prior to use of new technologies has also been addressed by Rosen and Mays in the context of the British National Health Service [20]. They note that while one option is to control technology while research is conducted to assess clinical and cost effectiveness, pressures for diffusion from various sectors make such control difficult. They suggest that the horizon scanning program should improve the capacity to start evaluating emerging technologies as they are developed. Like Forrester et al. [9], they draw attention to the dynamic nature of many new technologies, with refinements being undertaken in response to the experience of early users. Current methods for research synthesis can discriminate against early studies which are unlikely to meet criteria for systematic reviews, and RCTs will not be available for meta-analysis. Policy makers may well have to depend on the results of observational studies in the first instance to make a judgement as to the eventual effectiveness of a technology.

Rosen and Mays [20] suggest the need for a more flexible and iterative approach to incorporate evolving research findings into policy on the early use of new technologies, and to help design subsequent studies. Similar points on the iterative application of economic evaluation have been made by Sculpher et al. [23].

Some technologies will be particularly problematical in terms of availability of good quality evidence. For example, Saver [22] draws attention to developments in chemotherapy, with different drugs being used at changing dose levels and time intervals. Combined modality therapy may be difficult to assess. A similar point is made by Wood [26] regarding the difficulties that may arise through using devices in combinations that have not been fully evaluated for safety. As an illustration, two devices which had received FDA approval were used together in a defibrillating system whose longer term safety had not been evaluated.

Wood [26] comments on the inadequacy of early data on the efficacy and cost-effectiveness of medical devices. As clinical trials may be small, " physicians are forced to make judgements about the use of new technologies based on incomplete information on effectiveness and appropriateness". If there is uncertainty, new technology will not entirely replace existing approaches and in fields such as the management of cardiac disease, redundant tests will be obtained. Older procedures may be slow to disappear from service.

Within Canada, Health Canada has a role in obtaining information on some types of technologies that may be useful in determining whether the status of 'experimental' is applicable.

Basis of coverage decisions

In a survey of private US health plans, Steiner et al. [24] found that the most frequently sources of information used were medical journals, opinions of local experts, FDA clearance documents and information from health plan associations. Almost all responding medical directors (95%) listed evidence from RCTs as important in decision making. Interestingly, meta-analysis ranked second at 60%, with reviews at 45%. Only RCTs were viewed by the majority of medical directors as sufficient to use alone when making a policy decision on whether to cover a new medical technology. Half did not list medical journals as being used, in part because often there are only small numbers of articles in peer-reviewed journals at the time new technologies emerge.

Sabin and Daniels [21] have recommended that three conditions should apply to limit-setting decisions. These are that the rationale for the decision is clearly stated and publicly available; the rationale must make clear how the policy supports providing "value for money" in meeting varied health needs of a defined population under reasonable resource constraints; and that there is a

mechanism for challenge, dispute resolution and introduction of new facts and arguments.

Diamond (citing Eddy) [7] mentions that a coverage decision should stress the following:

- Coverage applies to a health treatment intervention for a medical condition.
- Sufficient evidence of value exists to indicate that the intervention has a positive effect on health outcomes and will have the intended effect in this case.
- The benefits of the intervention are clear.
- The therapeutic intervention can be delivered cost-effectively.

Diamond [7] makes a distinction between coverage decisions and practice guidelines in terms of their use of evidence and professional judgement. In coverage decisions the focus is at the group level and for clinical practice guidelines at the individual patient level. However, one of the difficulties for decision makers in Alberta is that often judgements on new technologies are being called for at both levels; requests in respect on single and small groups of individuals are common. Diamond [7] also suggests a policy of temporary coverage decision making, with a defined process.

Gleeson [10], Saver [22] and Belk [3] draw attention to criteria used by the Blue Cross Blue Shield Technology Evaluation program which are focused on the effect of a technology on health outcomes. The program assesses whether a technology meets the following five criteria:

1. The technology must have final approval from the appropriate government regulatory bodies (not applicable to procedures).
2. The scientific evidence must permit conclusions to be drawn concerning the efficacy of the technology based on health outcomes (emphasis on well designed and conducted investigations published in peer-reviewed journals).
3. The technology must improve the net health outcome (benefits must outweigh any harmful effects).
4. The technology must be as beneficial as any of the established alternatives.
5. The improvement must be attainable outside an investigational setting.

Gleeson [10] notes that the Blue Cross Technology Evaluation Center (TEC) does not make recommendations on a technology's eligibility for coverage only whether it meets TEC criteria. Blue Cross Plans may consider technologies that do not meet the five TEC criteria to be investigational and not eligible for coverage.

Aubry [1] comments that economic analysis is not part of the Blue Cross Blue Shield criteria for evaluation of clinical effectiveness and that the heart of the criteria is the second point. He notes that a number of diagnostic technologies have been evaluated against these criteria and a key issue is the need to demonstrate that testing leads to improved health outcomes via a change in treatment or management.

Braslow et al. [4] have outlined a similarly-based process used by United HealthCare (see Figure 1). Again, emphasis is placed on regulatory approval, effect on net health outcomes and whether the technology is of greater value than available alternative methods.

Figure 1: United HealthCare review process stages

United HealthCare review process stages:

1. **Is the technology experimental? ***
2. **If not, does the technology improve net health outcomes?**
3. **If yes, is the technology non-cosmetic and required for reasons other than convenience?**
4. **If yes, is the technology of greater value than conventional therapy?**
5. **If yes, the technology is eligible for coverage**

***On the basis of FDA definitions/ approval, drug compendia listing for drugs and devices; evidence from clinical studies for procedures.**

Source: reference Braslow NM, et al. [4].

Young [27] discusses the interaction of the FDA approval process with off-label use of drugs for the treatment of cancer. At issue is whether the early use of a drug is identified as clinical research or that early access to a drug is considered since it is likely to be successful. He makes a number of recommendations, suggesting expeditious clinical trials that are peer-reviewed in phases I and II; giving early access to new treatment through an appropriate protocol and considering off-label use of an approved drug as a modality of therapy rather than clinical research. Clinical research should not excuse access to care.

McCabe [14], in discussing availability of cancer treatments, draws attention to the continuum of knowledge as trial results become available, so that the distinction between experimental and standard therapy become blurred. It is argued that non-coverage of costs related to use of investigational therapy may adversely affect trial design and prevent access of many patients to promising new treatments.

Eddy [8] notes that in the US, the objective of coverage criteria is frequently misunderstood. "A common view is that coverage criteria are a club by which plans try to deprive members of treatments they want". Coverage criteria developed at a workshop sponsored by the National Institute for Health Care Management [15], are listed by Eddy.

> Health plans are required to cover health interventions within the specified benefit categories if they meet the following criteria:
>
> 1.1. The intervention is used for a medical condition.
>
> 1.2. There is sufficient evidence to draw conclusions about the intervention's effects on health outcomes.
>
> 1.3. The evidence demonstrates that the intervention can be expected to produce its intended effects on health outcomes.
>
> 1.4. The intervention's expected beneficial effects on health outcomes outweigh its expected harmful effects.
>
> 1.5. The intervention is the most cost-effective method available to address the medical condition.

Eddy [8] has drawn attention to the difficulty in finding the appropriate level of detail in developing coverage criteria: "Benefit language must serve two conflicting purposes: on the one hand, it should be precise, which implies technical language and lots of details; on the other hand, it should be accessible and comprehensible, which implies non technical language and brevity".

Braslow [4] mentions the response by health plans to limit new technology to strict indications. Health plans may specify provision only within academic centres to replicate the research environment or offer time limited coverage and reassess the technology once sufficient experience has been gained in clinical practice.

Use of expert opinion

Saver [22] notes that the more novel the technology, the less likely it is that experts will have sufficient background to adequately inform the 'trier of fact'. Eddy [8], in discussing the coverage criteria listed above, notes the requirement "that our beliefs about an intervention be anchored to empirical evidence, not expert judgment, professional consensus, or common usage."

Role of health technology assessment

Saver [22] concludes in his review that assessments are not performed early enough or regularly enough in the technology development process. A goal of health technology assessment (HTA) is to facilitate the appropriate introduction and use of new health technologies. When applied to questions of whether a technology is experimental, HTA should be bringing to bear interpretation and synthesis of available evidence in a transparent, checkable fashion. In Rettig's [19] terms, HTA should sustain medical innovation while redirecting it towards cost-reducing, quality enhancing technical change.

These useful guiding principles, however, are not necessarily helpful in decisions on the introduction of some types of emerging technologies.

SECTION 2: OPINIONS OF ALBERTA DECISION MAKERS – A MODIFIED DELPHI STUDY

OPINIONS OF ALBERTAN DECISION - MAKERS

Views of decision makers in Alberta on definitions of experimental technology and their application were explored through a two round modified Delphi study undertaken by AHFMR [11, 12]. The objective was to develop criteria to define the status of new technologies from an assessor's perspective and how status might be linked to decisions on support based on another set of criteria identified through this study.

The panel of experts used in the study included medically qualified staff from Regional Health Authorities, the Alberta Medical Association, the College of Physicians & Surgeons and Alberta Health and Wellness. Criteria were developed by AHFMR on three dimensions: critical appraisal of the evidence, funding elements and elements for funding decisions. These criteria were pre-tested. The panel was requested to rank or rate the criteria, using a Likert scale. Only respondents from round one received material for round two. Thirteen persons completed responses to both rounds.

Means (M) and standard deviations (SD) for responses to each statement were calculated. Missing responses to certain criteria statements were excluded from the computations. Consensus was defined prior to the study as a minimum of 60% agreement by panel members on any statement.

Criteria for determining status of a technology

Panel members were asked to rank the following nine criteria for determining the status of a technology as experimental, intermediate or established. Results based on the responses received are shown in Table 1 which indicates opinions on the status indicated by each criterion, ranging from One (established) to Five (experimental).

Criteria for determining status

A one well designed RCT, statistically significant (SS) benefit

B two to three well designed RCTs, SS benefit

C one well designed RCT with a positive result but not SS

D two to three well designed RCTs with a positive result but not SS

E several controlled studies, SS result but uncertain clinical benefit

F several controlled studies, no SS result but promising clinical benefit

G no controlled studies, several case series (cumulative total <20 cases) with positive results and findings supported by expert opinion

H no controlled studies, several case series (cumulative total >20 but <50 cases) with positive results and findings supported by expert opinion

I several controlled studies with results that had statistical and clinical significance.

Table 1: Opinions on criteria for defining technology status

Criterion	Opinion on the status of a technology					Result
	One	Two	Three	Four	Five	
A	0/13	4/13	8/13	1/13	0/13	92% intermediate/established M 2.8 SD 2.17- 3.37
B	4/13	9/13	0/13	0/13	0/13	92% established M 1.7 SD 1.21-2.17
C	0/13	0/13	3/13	7/13	3/13	77% experimental/intermediate M 4.0 SD 3.29-4.71
D	0/13	2/13	3/13	7/13	1/13	77% experimental/intermediate M 3.5 SD 2.66-4.42
E	0/13	1/13	9/13	3/13	0/13	85% intermediate/experimental M 3.2 SD 2.60-3.71
F	0/13	1/13	6/13	5/13	1/13	85% intermediate/experimental M 3.5 SD 2.69-4.24
G	0/13	1/13	4/13	3/13	5/13	62% experimental M 3.9 SD 2.89-4.96
H	0/13	3/13	2/13	7/13	1/13	69% experimental/intermediate M 3.5 SD 2.49-4.43
I*	8/9	1/9	0/9	0/9	0/9	100% established M1.1 SD 0.78-1.44

*Only nine complete responses received for this criterion

Criteria for elements in funding decisions

Panel members were requested to rank several elements that should be considered in funding decisions. The following order of priority was indicated by the participants:

1. levels of benefit compared to alternative intervention;
2. quality of life or functional status;
3. survival advantage;
4. regulatory status in Canada or the USA;
5. overall cost to health care system;
6. severity of condition; and
7. availability of expertise, skills facility.

There was no consensus on the ranking for an element relating to appropriate number of individuals.

Criteria for funding

Panel members were asked to rank the following criteria to support or not support funding technologies:

A no final regulatory approval, is the only alternative available which may affect survival and quality of life

B promising beneficial results for a serious life threatening condition, not supported by scientific evidence, available out-of-province

C promising beneficial results for a chronic, non-life threatening condition, not supported by scientific evidence, available out-of-province

D beneficial effects in terms of quality of life are more significant than current intervention but do not affect the disease process

E beneficial effects in terms of quality of life are more significant than current intervention but do not affect the disease process and are more costly

F beneficial effects are less significant than available intervention and less costly

G beneficial effects and costs are the same than available intervention

H beneficial effects are more significant and more costly as alternative intervention appropriate for >500 individuals

I beneficial effects are more significant and more costly than alternative intervention appropriate for <100 individuals

Results are shown in Table 2, with opinion ranging from One (fund) to Five (do not fund).

Table 2: Opinions on criteria for funding technologies (bolded indicates summation)

Criterion	Opinion on whether to support funding					Results
	One	Two	Three	Four	Five	
A*	0/11	7/11	3/11	1/11	0/11	64% fund M 2.5 SD 1.77-3.14
B	0/12	4/12	**3/12**	**4/12**	3/12	64% do not fund M 3.3 SD 2.10-4.56
C	0/12	2/12	1/12	2/12	7/12	64% do not fund M 4.2 SD 2.97-5.36
D	**4/12**	**5/12**	2/12	1/12	0/12	75% fund M 2.0 SD 1.05-2.95
E	2/12	**5/12**	**5/12**	0/12	0/12	83% fund M 2.3 SD 1.05-3.00

Table 2: Opinions on criteria for funding technologies (bolded indicates summation) **(cont'd)**

Criterion*	Opinion on whether to support funding					Results
	One	Two	Three	Four	Five	
F	0/12	1/12	**5/12**	**4/12**	2/12	75% do not fund M 3.6 SD 2.68-4.48
G	0/12	1/12	2/12	**3/12**	**6/12**	75% do not fund M 4.2 SD 3.14-5.20
H	**5/12**	**7/12**	0/12	0/12	0/12	100% fund M 1.2 SD 1.07-2.10
I	0/12	9/12	3/12	0/12	0/12	75% fund M 2.3 SD 1.80-2.70

*No response or zero preference not included

Application of criteria to specific technologies

Application of the criteria to four health technologies is illustrated in Table 3. The results draw on the weights given by the opinions of the panel to various criteria.

Table 3: Status and funding recommendations for four technologies

Technology	Status	Other considerations	Funding recommendation
Air plethysmography for venous evaluation	**Experimental** -due to lack of evidence (from controlled studies).	Other diagnostic tests available. This technology is non invasive, regulatory status in Canada bears little weight	**Do not fund**
Cord blood transplantation for adults	**Experimental** - lack of evidence, (no controlled studies; only one case study)	Other alternatives available - bone marrow transplantation. And peripheral blood transplantation.	**Do not fund**
Percutaneous ethanol injection therapy for hepatic cancer	**Intermediate** - one RCT with statistically significant (SS) benefits	Beneficial effects in terms of quality life are more significant than alternatives and it is less costly	**Fund**
Posteroventral pallidotomy in Parkinson's Disease	**Intermediate** - one prospective controlled study and several prospective case series with SS benefits	effects in terms of quality of life are more significant than other interventions but does not affect the disease process	**Fund**

Opinions from the panel members seemed consistent in regard to definition of criteria for established technology, being guided by views on the importance and availability of good quality controlled trials. Opinions were more varied on definition of intermediate or experimental technology.

With the criteria for elements in funding decisions, levels of benefit from the technology including effects on quality of life or functional status and survival advantage ranked highly. Regulatory status of the technology, cost to the health system, severity of the condition and availability of expertise were seen as less important.

Responses on criteria again suggested concern regarding benefits from the technology, rather than cost, with some indication that numbers of persons using the technology might also be a factor.

It was concluded that use of simple criteria for defining experimental or not adequately validated technologies can assist the decision-making process of agencies responsible for providing coverage of funding for health care services.

SECTION 3: CONCLUSIONS FROM AHFMR ASSESSMENTS

FURTHER INDICATIONS FROM AHFMR ASSESSMENTS

A further indication of issues on emerging technologies from the HTA perspective can be obtained from consideration of the conclusions reached in a number of assessments undertaken by the AHFMR HTA program. The assessments all involved some discussion or consideration of the status of the technology under review, though explicit statements as to whether the technology was experimental were not necessarily included. In the examples given here, 27 technologies were considered in 37 reports. Further details are given in Appendix B and the titles of the reports are listed in Appendix C. Both full assessments and shorter, unrefereed reports (Technotes) are included.

Review of these assessments and their recommendations indicates that decisions on the status of a technology and the support for it may often be complex, with a number of issues needing to be taken into account.

The technologies fall into four groups. In the first, each of the technologies being assessed had a single application and there were issues regarding its status. The next two categories comprise technologies with multiple applications, and groups of technologies used for a particular application. Finally, some older technologies are considered, which were not experimental but which required decisions on the method and extent of use.

The status of each technology can be assigned as experimental, not adequately validated or established, with definitions consistent with those used in the Delphi study. 'Experimental' is taken to mean that there is no better than weak evidence of efficacy, typically associated with an absence of good quality studies. Experimental status is also typically associated with use of the technology on relatively small numbers of patients or clients.

'Not adequately validated', corresponding to 'intermediate' used in the Delphi study, is taken to mean that evidence of efficacy, effectiveness or safety is in some respects limited so that substantial uncertainty remains over the performance of the technology in the health system. Use of technologies in this category may have become widespread. While the concerns regarding lack of good quality evidence of benefit remains, it is difficult to apply the 'experimental' description to modalities that may have been applied to large numbers of people.

Conclusions or recommendations in each assessment indicated whether the technologies in question should be supported, conditionally supported or not supported. Conditional support refers to the situation where funding or other endorsement of the technology is linked to requirements such as collection of data for further validation, restriction on numbers or types of patients, or assurance of adequate skills and training.

Overall judgements taken on the technologies considered are shown in Table 4, and reflect the information that was available at the time that each assessment was completed. Three of the technologies fell under more than one classification of status, such that a total of 30 results are listed. Recommendations on support did not necessarily follow the status of the technology.

Table 4: Decisions in AHFMR assessments on status and support for technologies

Status of technology	Total	Supported	Conditionally supported	Not supported
Experimental	14	3	5	6
Not adequately validated	14	5	7	2
Established	2	2		
	30	**10**	**12**	**8**

In each case, the status of the technology was judged on the basis of the extent and quality of the evidence available in the literature, and from other sources. Recommendations on support made in the assessments were informed primarily by the strength of the evidence, the severity of the disease or condition for which the technology was used and by the availability and performance of alternative technologies available in the Alberta health care system. Expected caseload and the costs of the technology were not major factors in most of the HTA decisions, though they might well be of importance to decision-makers in policy or program areas.

Technologies supported by AHFMR assessments are listed in Table 5 with indications of severity of condition, available alternatives, caseload and costs. Caseload and costs are given in indicative terms which are not firmly specified. However, a caseload of more than 5,000 could be regarded as high and high cost technologies might include those of over $3,000 per case.

For the experimental technologies, the conditions being treated were severe. There are alternatives to cord blood transplantation, but these are not readily available to some patients. Adult extra corporeal membrane oxygenation (ECMO) is a technology of last resort for some patients with respiratory failure, and the alternatives are of unknown efficacy. Pallidotomy is a treatment for persons with Parkinson's Disease for whom drugs are no longer effective and whose other management options are poor.

For the two technologies that were not adequately validated, measurement of bladder urine volume by ultrasound provided a safer approach to an invasive alternative (catheterisation) and percutaneous ethanol injection therapy (PEIT) for liver cancer is an approach to treatment of a severe illness were lacking adequate established management options.

Of the older technologies in Table 5, the first three had limited evidence of effectiveness, on the basis of literature reports, but provided reasonable approaches when compared with the options available to the patients concerned. Hyperbaric oxygen treatment has been used for many conditions but was supported only for those where there was good evidence of effectiveness or where it was overwhelmingly accepted as the standard of care. Use of IVF was supported only for cases of infertility due to Fallopian tube blockage.

Table 5: Technologies supported by AHFMR assessments

Technology	Condition severity	Alternatives ?	Number of cases	Costs
Experimental				
Cord blood transplant	High	Yes, but limited access	Low	High
Adult ECMO	High	Yes, efficacy unclear	Low	Moderate-High
Pallidotomy	High	Yes, but poor options	Low	Moderate
Not adequately validated				
Bladder ultrasound	Moderate	Yes, but invasive	Low-moderate	Low
Percutaneous ethanol infusion	High	None established	Low	Low
Older technologies, not adequately validated				
Sex reassignment surgery	Moderate-High	Yes, but ineffective in severe cases of dysphoria	Low	High
Electrical stimulation, fractures	Moderate – High	Not well validated	Low	Moderate - High
Implantable infusion pump, MS	Moderate-High	Yes, but efficacy varies, compliance problems	Low	Moderate-high
Established technology				
Hyperbaric oxygen treatment [a]	Moderate-High	In some cases	Low	Moderate-High
In vitro fertilization [b]	Low – moderate	Yes, low effectiveness for some cases	Low-Moderate	High

Notes: a - refers to use in six conditions where there is good evidence of effectiveness

b - refers to use in one type of infertility where there is good evidence of effectiveness

Table 6 lists those technologies for which there was conditional support in the assessments. For each of the experimental technologies, recommendations for future support were linked to further studies and/or collection of data, some at the local level. Generally, these approaches were seen as offering promise for management of serious conditions where there were no established alternatives.

Collection of additional data was also recommended for all of the not adequately validated technologies. In addition, skill-related requirements were noted for cabromab pendetide.

Table 6: Technologies conditionally supported by AHFMR assessments

Technology	Condition severity	Alternatives ?	Number of cases	Costs
Experimental				
Pressure measurement devices	Moderate	Not for quantitative measurement	Potentially high	Moderate
Gait analysis	Moderate – High	Yes, limited utility	Low	High
Lung volume reduction surgery	High	Effectiveness limited	Low-Moderate?	High
Cryosurgery, prostate cancer	High	Various	Moderate	Moderate
Experimental				
Dynamic posturography	Moderate	Various, non-quantitative	Potentially high	High
Not adequately validated				
Brachytherapy, prostate cancer	Moderate-high	Various	Moderate	Moderate
Cabromab pendetide	High	Various, but some limitations	Moderate	High
Radiosurgery	Moderate-High	Microsurgery & others	Low	Moderate-High
Vagus nerve stimulation	High	Poor	Low	Moderate - High
Telepsychiatry	Moderate – High	Face to face consultation	Low-moderate	Moderate
Functional diagnostic imaging[a]	High	Poor	Low	Moderate - High
Older technology, not adequately validated				
Tests for vaginitis	Low – High	Various	High	Low

Note: a.- Conditional support for some imaging technologies where there was limited evidence of benefit in management of refractory epilepsy or symptoms of heart failure

The technologies for which the assessments did not recommend support are listed in Table 7. For the first three experimental technologies, there were established, reasonable alternatives and the value of any additional information offered by these diagnostic methods did not seem compelling. The others in the experimental category are multi-application technologies also listed in Tables 5 or 6. The status of experimental technologies has been applied to their use in particular applications.

Low level laser therapy for wound healing has been widely used, but does not have regulatory approval, evidence of benefit is weak and effective alternatives are available.

The remaining entry, aspirin in primary prevention of cardiovascular disease and colon cancer, provides an example of an established, widely used technology which is not recommended for support in a particular application given uncertainty as to whether its benefits would outweigh its adverse effects.

Table 7: Technologies not supported by AHFMR assessments

Technology	Condition severity	Alternatives ?	Number of cases	Costs
Experimental				
Air plethysmography	Moderate	Yes	Moderate	High
Laser ophthalmoscope	Moderate	Yes	High	?Moderate
Ultrasonic bone density measurement	Low-Moderate	Yes	High	Low
Hyperbaric oxygen [a]	Moderate-high	For most conditions	Moderate	Moderate to High
In vitro fertilization [b]	Low – moderate?	Low effectiveness for some cases	Low-Moderate	High
Functional Diagnostic Imaging[c]	High	Poor	Low	High
Not adequately validated				
Lasers in wound healing	Moderate	Yes	High	Low
Older technology, not adequately validated				
ASA in primary prevention	High	Yes - lifestyle-related	High	Low

Notes a - refers to applications of HBOT where there is not sufficient evidence of effectiveness
b - refers to use of IVF for infertility due to causes other than Fallopian tube blockage
c - refers to imaging modalities for which there is not adequate evidence of efficacy in the applications considered

There was general agreement between the assessments and the analysis following the Delphi study on the status and support for the four technologies

mentioned in Table 3. The difference in regard to support for cord blood transplantation arises from the Delphi study analysis considering only one application of this technology (transplantation in adults) for which there was minimal evidence of benefit at the time.

These examples bring out some further points during consideration of whether or not a technology should be considered as experimental:

- Technologies may be well established and widely used, but still experimental in a particular application. As well as the aspirin example listed in Table 7, implantable infusion pumps are well established technology - it was the particular application to management of spasticity in patients with multiple sclerosis that was in question.
- Technologies may be widely used, but have poor levels of evidence and substantial variation in how they are used. Both additional studies and guidelines on standards of practice may be required. Tests for vaginitis and electrical stimulation for fracture healing provide examples.
- In some cases, there may be uncertainty because of the lack of data due to the long term nature of the condition being treated, or to the complexity of the issues involved. Definitive information on the effectiveness of brachytherapy for treatment of prostate cancer is unlikely to emerge for some considerable time. Sex reassignment surgery for gender dysphoria is a highly complex area, where effectiveness of the intervention is difficult to establish.
- Some technologies may need to be considered in terms of their use in combination with other approaches. This was the case with the functional diagnostic imaging methods and the tests for causes of vaginitis.
- Cost considerations were not a major factor informing the recommendations on support in most of the assessments, which focused on questions of efficacy/ effectiveness and safety. However, the reports on stereotactic radiosurgery and telepsychiatry both included cost analyses that informed the position taken. In each case, there was a comparative analysis of different versions of the technology or of different options for consultation using a cost minimisation approach.

In another assessment, a cost analysis established that cord blood transplantation was more expensive than other approaches to allogeneic stem cell transplantation, though this was not seen as a reason to recommend against support for the technology. Cost considerations also informed the conclusions of the reports on functional diagnostic imaging and percutaneous ethanol injection therapy, though there were no cost analyses.

SECTION 4: SUGGESTIONS FOR DECISION MAKERS

FURTHER DEVELOPMENT OF CRITERIA FOR DECISION-MAKERS

The concepts developed by AHFMR for the modified Delphi study and the approaches in the individual assessments parallel a number of points made in the literature available for review. The status of a health technology, as experimental or otherwise, is largely determined by reference to the scientific literature on its efficacy and safety. There is then a further set of considerations on how to proceed once the technology's status is determined.

There are variations in opinion on definition of 'experimental' and the strictness of application of rules of evidence seems to vary. While, in principle, evidence from good quality trials should be a requirement to move the status beyond 'experimental', practical difficulties may arise if the technology has had very wide use or if some aspects of its performance have been well investigated. In Germany, widespread use and reasonable scientific discussion in support of a technology are factors that may influence funding decisions (Gibis, personal communication). It may often be useful to term a technology as 'not adequately validated', recognising that in some sense it has moved beyond being experimental but that some concern regarding its efficacy, effectiveness or safety remains.

Consideration of coverage for a technology might then proceed with reference to a framework set by the questions:

1. Is the technology experimental?
2. If not experimental, is it adequately validated?
3. If experimental, or not adequately validated, what other clinical criteria should be considered?
4. What economic and other considerations should also be taken into account?

Figure 2 summarises some issues that may need to be considered in each of these areas.

Figure 2: Points to consider in determining status of a health technology and its suitability for support

A. Whether still experimental

1. Human use
2. Number of persons who have received the intervention
3. Level of evidence of efficacy
   *trial design
   *power, quality of study
   *length of follow up
4. Approval by major regulatory agency

B. Whether adequately validated if not experimental

1. Long term, widespread use but poor quality of evidence (study design, outcomes measurement, length of follow up)
2. Available evidence not relevant for the indication in which the technology is to be used
3. Available evidence not relevant to patient population

C. Factors affecting HTA recommendations on support

1. Nature of disease or condition; population affected
2. Performance and availability of alternative technologies
3. Incremental benefit expected – significance/dominance of technology in management of the disease or condition
4. Availability of adequate competency, infrastructure

D. Further considerations for decision-makers

1. Effect on specific budgets
2. Potential cost – effectiveness of the technology
3. Access and equity for those requiring the intervention

Is it experimental?

There seems general agreement that definitions of 'experimental technology' have some limitations for decision-makers. In reality, there will be a continuum between the clearly experimental, for example first use in human trials, and a different status as the technology moves into wider use. Also, as Reiser [18] points out, once technologies are placed in the standard or experimental category, they do not reside there undisturbed. Decision-makers will need to take note of new

findings and bear in mind that classification of the status of technologies is a dynamic process.

Approval by a major regulatory agency, such as Health Canada or the FDA may be a useful indication of status. It is suggested, however that this attribute be used as a guide only as there will be a need to consider the nature of the approval for a specific product and the extent to which this is generalisable to the situation facing decision-makers in the health care system.

As indicated in Figure 2, numbers of persons who have received the intervention may be a factor in deciding whether it is experimental, in addition to the various components contributing to the level of available evidence on efficacy.

If not experimental, is it adequately validated?

There may well be compelling reasons to have concern at the performance of a health technology, even though it is no longer experimental. Very commonly, technologies come into widespread use before there are definitive data on their efficacy and safety. Decision-makers may well form the view, taking all available information into account, that proponents of a non-experimental technology still have a case to answer and that support is not appropriate until further evidence emerges. As indicated in Figure 2, problems may arise if the available evidence is not relevant to the local patient population or to the setting within which the technology is to be used. In this case 'Not adequately validated' may provide a useful description.

On the other hand, definitive information on a technology will often take many years to emerge. Decision-makers will need to consider how much assurance about the attributes of a technology is really needed before support for its use is approved. As noted earlier, it has been argued that delay in providing support for a technology will disadvantage the health system through impeding the diffusion of new and more effective interventions.

Reiser [18] notes that the decision that an experimental technology has reached the point of becoming standard practice is played out in many venues and that such decisions will reflect considerations based not only on science but also on social influences.

Factors affecting HTA recommendations on support for a technology

As indicated previously, the seriousness of the disease or condition for which an emerging technology is to be used will be a factor influencing the position taken in a health technology assessment on whether it should be supported. There must be some reasonable indication that the new technology will be capable of producing benefit, regardless of the severity of the disease. However, if the disease is serious then there may be reasonable argument to introduce the

technology relatively quickly, making judgements on possible benefits to the group of patients concerned on the basis of limited evidence. Support for a technology in such circumstances may be conditional and linked to subsequent provision of additional data on its performance.

The availability of alternative technologies for managing the disease or condition, and their effectiveness in that role, will be major influences on the position taken in health technology assessments. If the technologies that are already available within the health care system are known to be effective for use in managing a condition, then there will be less compelling reasons for introducing an emerging technology, especially when there are few data on its efficacy and safety.

Both assessors and decision-makers will also need to consider the significance of the technology in the disease management algorithm. It may be that an emerging technology shows promise, but has a minor role in management of a condition and may provide only a small incremental benefit.

Finally, both assessors and decision-makers may need to consider the availability of adequate competency within the health care system in the operation of the technology and the availability of necessary infrastructure to support its use.

Further considerations for decision - makers

Those who are responsible for funding decisions in the health system will typically be interested in cost issues related to the emerging technology. The effect of support for a technology on specific budgets may well be of immediate concern. Taking a broader perspective, cost effectiveness of the technology in a particular application will be important in informing decisions on support.

Advice on cost effectiveness may be provided by the health technology assessment, but typically economic data will be sparse in the early stages of life of a technology. Decision-makers may be faced with having to make provisional judgements on likely cost-effectiveness in the absence of good quality data and analysis. They may also need to bear in mind that indications for some technologies may widen following introduction.

Decision-makers within health authorities, professional groups and institutions may also need to pay close attention to whether there will be reasonable access to the emerging technology for those whom it might benefit. If there is to be rationing of the technology, then criteria for its use will have to be developed, and made explicit.

OPTIONS FOR DECISION-MAKERS

Issues related to the classification and support of new technologies are complex. The view that has been put forward here is that there are two sets of decisions that need to be considered. The first relates to whether a technology should be regarded as 'experimental' and the other to whether its use in a health care system should be supported and under what conditions. Classification of a technology as 'experimental' does not necessarily mean that support for its use should be denied. The frameworks developed by several organisations in the USA provide useful guidance, but may need some adaptation for local conditions.

The main guide as to whether the 'experimental' classification should be applied to a technology is the quality of the available evidence of safety and efficacy, using the principles that are widely applied in health technology assessment. However, as indicated in some of the papers reviewed, there are difficulties in obtaining high quality data on efficacy of some technologies over short time periods. In practice, decision makers may need to take judgements on support for emerging technologies on the basis of limited evidence.

From the HTA perspective, however, severity of the condition, number of individuals appropriate for the intervention, and availability and performance of alternative technologies are also major factors in considering whether a technology that is 'experimental' or 'not adequately validated' should be recommended for support. Comparison to the performance of alternative technologies implies that pertinent evidence of efficacy is available. In other words, it is assumed that the alternatives have proven to be efficacious and effective. Decision makers will also have to consider regulatory status, costs and other factors including legal, social and ethical issues related to the programs that they are administering or advising.

Information gathered on these various issues can then be used to inform a policy decision on support for the technology. Synthesis of the available information might be undertaken at different levels. A basic approach is suggested by the decision matrix outlined in Table 3, which brings together elements of technology status and benefits in comparison to alternative technologies. Possibly, weights could be given to different attributes to produce a numerical index as a guide to decisions. For example, status of the technology, severity of the condition being managed, and benefit from alternative technologies might be ranked in terms of possible desirability of support.

However, such approaches, even if refined further, can provide only the most basic of guides to decisions on whether to support emerging technologies. The synthesis process is likely to remain complex, with other attributes and issues making an important contribution in many cases.

As suggested in several of the reviewed papers, and by the recommendations associated with AHFMR assessments, conditional support may often be proposed for an 'experimental' or 'not adequately validated' technology. Options for future action by the funding authority might include:

- Introducing general financial support, for example through a schedule or through grants.
- Denying support if there are strong indications that the technology is ineffective, or if there are adequate alternative technologies available.
- Providing support in the context of a local primary study
- Providing limited support, conditional on collection of outcomes data or on restriction to a sub-population of potential clients.
- Denying support for the time being, pending a future review of evidence reported in the literature.

If conditional support is linked to requirements for collection of additional data, there will be a need for active management of future coverage for the technology by the funding body (for example a health authority) perhaps in association with an HTA program. Decision - makers will have to think beyond a basic 'gate keeping' response to the classification of a technology. Further developments in the technology and additional clinical findings should be taken into account. Also, the decision making organization will need to be prepared and able to rescind or modify the conditional approval if subsequent information on the technology does not confirm initial indications of efficacy, or if requested data collection is not implemented.

This paper has addressed two questions: the meaning of 'experimental' from an assessor's perspective and the question of coverage of emerging technologies with reference to the needs of the decision-maker in areas responsible for procurement and funding. Patients, health care professionals and manufacturers are likely to have somewhat different perspectives on a number of the issues discussed here. There would, for example, often be a greater emphasis by these groups on the early availability of emerging technologies. However, the various factors considered here should also be useful to these groups in contributing to more transparent decision-making and in helping to identify key attributes of health technologies that require consideration by all parties.

APPENDICES

APPENDIX A: METHODOLOGY

Relevant English language papers related to definition and coverage of emerging health technologies were sought in the following databases: HealthStar [1975-1999], EMBASE [1988-1999] Bioethics Line [1972-1999], Medline (1966-1999), Current Contents [1998 to April 24, 1999] Canadian Research Index (1982-1998), and the CRD HTA Database. Non-human studies were excluded.

Subject Headings included Technology Assessment, Biomedical/ Insurance Coverage/ Device Approval/ Decision Making Insurance, Health, Reimbursement/ Reimbursement Mechanisms/ Diffusion of Innovation/and Experimental Medicine. Keywords, which were used alone or in combination included experimental, cutting edge, unproven, new technology, unknown effective, promising, status of intervention, experimental tech, emerging tech, investigational technology, reimbursement.

From the papers identified, a selection was made to include those that included discussion on definition of experimental technology and on criteria for selection of emerging technologies for reimbursement or other support that appeared to be of relevance to the Alberta health care system. Publications dealing with reimbursement mechanisms and with legal aspects related to coverage decisions on health technologies were not considered.

Details of AHFMR assessments were obtained from review of the reports considered in this paper.

In this publication:

Efficacy refers to the performance of a technology under 'ideal' conditions or conditions of best practice; and

Effectiveness refers to the performance of a technology under 'routine' conditions, for example when it has become widely distributed in a health care system.

Appendix B: Characteristics of Technologies Considered in some AHFMR Assessments

Abbreviations:

AMI	acute myocardial infarction
APG	air plethysmography
ASA	aspirin
AVM	arteriovenous malformation
BMT	bone marrow transplantation
DEC	dobutamine echocardiography
DXA	dual x-ray absorbtrometry
EBRT	external beam radiation therapy
ECMO	extra-corporeal membrane oxygenation
EEG	electroencephalography
FDI	functional diagnostic imaging
fMRI	functional magnetic resonance imaging
GVHD	graft versus host disease
MEG	magnetoencephalography
MRS	magnetic resonance spectroscopy
MS	multiple sclerosis
PET	position emission tomography
PVP	posteroventral pallidotomy
QOL	quality of life
QUS	quantitative ultrasound
SPECT	single photon emission tomography
vs	versus

Table 8: Characteristics of technologies considered in some AHFMR assessments

Technology	Nature of disease, application; alternative technologies	Level of evidence, numbers of patients/ clients	Other considerations	Status, recommendation on support
Single application, decision on status				
Posteroventral pallidotomy, Parkinson's Disease	Population with compelling need for treatment (refractory to drug therapy). Poor alternative options.	Weak evidence, no controlled studies, though good indication of short –term effect; 100s of patients; limited follow up	Cost probably reasonable in comparison to alternative management options	**Experimental -** **Supported,** ongoing local data collection
Pressure measurement devices	Not dominant in management of severe condition (pressure sores)	Weak/ no evidence of effect on outcomes. Extent of use unclear	Cost could be daunting to users Several devices available	**Experimental -** **Conditional** – any support conditional on validation/ data collection
Bladder ultrasound for urine volume	Important for management of some types of patient. Indications that superior to catheterization	Limited comparative studies. ? 1000s of subjects	Appropriate training required	**Not adequately validated** **Supported**
Implantable infusion pump, Baclofen	Management of severe spasticity in MS through administration of Baclofen considered. Physical therapy, drugs, surgery options for treatment. Serious neurological complications associated with surgery.	Available studies had small patient numbers, variable design and variation in baseline and outcome measures. Use in several hundreds of cases	Context of use, patient selection need consideration.	**Not adequately validated** **Supported** - for use in carefully selected patients.
Gait analysis	Population (children with cerebral palsy or spina bifida) with walking difficulties and probability of multiple surgical interventions. Alternative methods of providing planning information to surgeons and others known to have major limitations	No controlled studies. Almost no information linking use of gait analysis to effect on management decisions or to effect on patient outcomes. At least several hundred children tested using this technology in various versions.	Lengthy test protocol; high expertise required. Expensive test, though potentially cost saving through avoidance of additional surgery.	**Experimental -** **Conditional** – link application to systematic collection and assessment of data on outcomes and costs.

Table 8: Characteristics of technologies considered in some AHFMR assessments (cont'd)

Technology	Nature of disease, application; alternative technologies	Level of evidence, numbers of patients/ clients	Other considerations	Status, recommendation on support
Single application, decision on status				
Percutaneous ethanol injection therapy	Unresectable liver cancer. No standard therapy for this small group of patients with poor prognosis	No adequate prospective controlled studies vs other treatment; one small RCT vs no treatment. > 1,500 cases reported in literature	Low cost, easily repeatable treatment with low morbidity.	**Not adequately validated** **Supported** - support for use in carefully selected patients with hepatocellular carcinoma. Do not support for treatment of hepatic metastasis
Telepsychiatry	Videoconsultation for various mental health conditions Alternative is face to face consultation	Survey data addressing mostly satisfaction, feasibility. Few data on longer term outcomes incl. mental heath status Now widely used	Still unclear of impact on overall mental health programs. Efficacy/ effectiveness closely linked to local organisational issues.	**Not adequately validated** **Conditional** - with appropriate data collection, as pragmatic help in coping with shortage of psychiatric services.
Cord blood transplantation	Leukemia and other hematopoietic disorders, particularly in children. Bone marrow transplantation (BMT) and peripheral blood stem cell transplantation alternatives.	No controlled or comparative studies; case series with small numbers of patients at individual centres. < 1,000 cases reported in literature	Alternative source of stem cells, giving treatment option for some individuals who would have little chance of BMT. Weak evidence of advantages over BMT in terms of possible degree of mismatch and severity of GVHD. Limited cell dose a disadvantage; some procedural matters not settled..	**Experimental -** **Supported** – promising, evolving technology, even though safety and efficacy not established.
Lung volume reduction surgery	Palliative treatment for end stage emphysema. Alternatives have limited effectiveness or availability - smoking cessation, drugs, lung transplant	Fair to poor levels of evidence from uncontrolled studies. Emerging indications of improved function, QOL, for some patients up to 2y post op. Several hundred patients	Large RCTs in progress	**Experimental -** **Conditional** – conditional support might be considered for selected patients, in context of trial.

Table 8: Characteristics of technologies considered in some AHFMR assessments (cont'd)

Technology	Nature of disease, application; alternative technologies	Level of evidence, numbers of patients/ clients	Other considerations	Status, recommendation on support
Single application, decision on status				
Cryosurgery for prostate cancer	Treatment of localized prostate cancer. Surgery, radiotherapy, brachytherapy are alternatives, plus hormonal treatment. Watchful waiting also an option	Several observational and retrospective studies, all with limited follow up data. RCT in progress. Several hundred patients in recent studies. Higher numbers with older versions of the technology.	Substantial morbidity associated with this technique. Several alternative management options, lack of comparative data on these.	**Experimental -** **Conditional** – support only in context of good quality clinical trial
Brachytherapy for prostate cancer	Treatment of localised prostate cancer, including recurrent cancer. Surgery, external beam radiotherapy, hormone therapy, watchful waiting alternatives.	Absence of controlled studies. Poor-fair evidence of effectiveness in short term, limited follow up with current versions of the technology. Long term efficacy unknown. Has been widely used, many thousands of cases.	Less invasive than prostatectomy, lower morbidity. Alternative technologies are continuing to evolve.	**Not adequately validated** **Conditional** – choice of treatment likely to be made on basis of physician and patient preference.
Cabromab pendetide	Diagnosis/ staging of metastatic prostate cancer. Complementary to other diagnostic tests, e.g. bone scans	No controlled studies. Poor-fair evidence of diagnostic accuracy, no firm data on effects on management or outcomes. Efficacy not established. Limited use; at least several hundred patients in the US	Has received FDA approval. High cost at $US 2,500 per test. For many patients, management decision might be taken on basis of other evidence	**Not adequately validated** **Conditional** - use may be indicated in a small number of selected patients.
Ultrasound for bone density measurement	Test for use in diagnosis and management of osteoporosis. X-ray methods, particularly DXA, widely used in this application.	Comparative data on devices available in Canada are limited, all have about the same level of precision, no data on accuracy. Little information on the use of QUS outside the research setting. Measures of performance in routine practice not yet available	Might provide option for use in under-serviced populations as alternative to DXA, but would need to consider confirmatory tests and potential duplication of services.	**Not adequately validated** **Not supported** - promising, but role in management of osteoporosis remains unclear. Further evidence required to establish place in routine health care.□

Table 8: Characteristics of technologies considered in some AHFMR assessments (cont'd)

Technology	Nature of disease, application; alternative technologies	Level of evidence, numbers of patients/ clients	Other considerations	Status, Recommendation on support
Single application, decision on status				
Air plethysmography	Test for investigation of venous function in lower extremities. Three other types of plethysmography also available.	No evidence on performance of APG in routine practice. Has been largely used in research. Most investigations were accuracy studies, patients as own controls. No RCTs, no study fully met criteria for methodological quality.	Can provide functional data that cannot be obtained from other methods, though accuracy and value of such information neeeds further study.	**Experimental -** **Not supported**
Low level lasers in wound healing	Use in treatment of wounds to accelerate healing. Other approaches include electrical stimulation, compression therapy etc.	Quality of evidence poor; studies include RCTs but with low numbers and some uncontrolled variables. Efficacy in this application is not established.	Not approved for this application by regulatory bodies. No generally-accepted and applied protocol for use.	**Not adequately validated** - (classification as experimental might be justified, though there has been widespread use). **Not supported** in absence of local primary data from well designed trials
ECMO in children and adults	Technology for use in cases of severe respiratory insufficiency. Mechanical ventilation is an alternative.	Quality of evidence limited and reflects circumstances of use; typically uncontrolled studies, small numbers of subjects. One RCT which found no difference from mechanical ventilation.	Context of use is in care of severely compromised patients with poor chance of survival. No consensus on appropriate use of the technique.	**Experimental** – **Supported** – for appropriately selected patients at centres with expertise.
Vagus nerve stimulation,	Refractory epilepsy Very limited options for this minority with condition refractory to drugs even following surgery.	Reasonable evidence of safety; results of good -quality RCTs indicated efficacy. Clinical significance not entirely clear. Patient selection criteria not established. Now thousands of cases.		**Not adequately validated** – (might justify experimental category) **Conditional** – support in context of closely controlled program, within formal study

Table 8: Characteristics of technologies considered in some AHFMR assessments (cont'd)

Technology	Nature of disease, application; alternative technologies	Level of evidence, numbers of patients/ clients	Other considerations	Status, recommendation on support
Single application, decision on status				
Laser ophthalmoscope	Diagnosis and monitoring of glaucoma Perimetry, tonometry and ophthalmoscopy routinely used in this application.	No data on performance in routine use; available data relate to research setting. Accuracy yet to be fully established. Further data needed on incremental benefits.	Potential advantages over established techniques. Incremental costs unclear.	**Experimental - Not supported**
Technologies with multiple applications, some requiring decision on status				
Hyperbaric oxygen treatment	Used/ proposed for many conditions. Often as adjunct to other therapeutic approaches.	Good evidence of effectiveness for use in 4 conditions, established standard of care in another 2. Limited evidence (Poor -Fair) for further 5 conditions, which does not support routine use. All other applications have only anecdotal/ single case support Widely used technology	Transport difficulties for some patients.	**Established** for some conditions. **Not adequately validated** or **experimental** in others. **Supported** for use in established applications **Not supported** in other applications
In vitro fertilization – embryo transfer	Treatment of infertility Other, less commonly used techniques of assisted reproduction	Most reports based on small uncontrolled studies, 2 recent RCTs. Many limitations in design, protocols, populations, outcome measures. Widely used technology.		**Established** – for severe bilateral tubal disease **Not adequately validated** or **experimental** for other indications **Supported** for bilateral tubal disease **Not supported** for other conditions.

Table 8: Characteristics of technologies considered in some AHFMR assessments (cont'd)

Technology	Nature of disease, application; alternative technologies	Level of evidence, numbers of patients/ clients	Other considerations	Status, Recommendation on support
Technologies with multiple applications, some requiring decision on status				
Computerized dynamic posturography	Rehabilitation of stroke, brain injured and amputee patients with vestibular/ balance deficits. Various other rehabilitation strategies in each of these groups.	No controlled studies of efficacy/ effectiveness for assessment and monitoring of patients in a rehabilitation setting . Evidence is fair to poor.	Reliability and validity of technology needs to be established for each patient group.	**Experimental -** **Conditional –** support only if use linked to data collection protocols, outcome measurement, patient selection criteria.
Stereotactic radiosurery	Benign tumours, AVMs, metastatic disease in brain; recent extension to treatment of lesions in neck, abdomen. Microsurgery option for many conditions; EBRT, brachytherapy for metastatic disease; embolisation for some AVMs.	Quality of evidence remains poor to fair across all applications; no RCTs, some case control studies. Used in a number of countries for many years. Many thousands of cases.	Comparative efficacy/ effectiveness of the two principal versions of the technology is not established; one is considerably cheaper than the other. High quality diagnostic imaging and treatment planning essential.	**Not adequately validated** **Conditional –** useful option for appropriately selected patients; support use cheaper version of technology, linked to collection of patient outcomes data.
Multiple technologies, some requiring decision on status				
Functional diagnostic imaging in epilepsy	Use of FDI methods (PET, fMRI, MRS, MEG) in management of refractory epilepsy. Other imaging methods, EEG used, limited benefit for some of this group of patients	No published RCTs to evaluate the diagnostic accuracy and impact None of the reviewed studies clearly met all the criteria for methodological quality	In the clinical situation, all would be used as complementary techniques to anatomical imaging methods such as MRI	**Experimental** - fMRI, MRS, MEG **Not supported** **Not adequately validated – PET Conditional** Only PET has a potential place in routine management. Possibly support in context of well designed studies on clinical impact

Table 8: Characteristics of technologies considered in some AHFMR assessments (cont'd)

Technology	Nature of disease, application; alternative technologies	Level of evidence, numbers of patients/ clients	Other considerations	Status, Recommendation on support
Multiple technologies, some requiring decision on status				
Functional diagnostic imaging, myocardial viability	Assessment of viability in dysfunctional myocardium as aid to treatment decision, PET, SPECT, MRI, DEC considered Earlier imaging techniques have limited role	Few good quality data on accuracy of the imaging methods in routine use, even fewer on their effect on patient management and outcome. No convincing evidence of benefit to health care.	These FDI methods remain technically challenging.	**Not adequately validated** or **experimental** in this application **Not supported** or **conditional** Any use should be associated with prospective studies involving long term follow up of patients
Tests for vaginitis	Diagnosis of causes of vaginitis symptoms Newer tests are under development	Primary studies of poor quality, which may not be generalisable. Tests have relatively poor diagnostic performance. Widespread general use.	Need for evidence on causal relationship between bacterial infections and serious gynecological/ obstetrical conditions.	**Not adequately validated** **Conditional support**, but require: Further work on accuracy of tests, criteria for analytical performance, Guidelines on current status, methods of use
Technologies that are not experimental, but which required decision on coverage				
Aspirin	Primary prevention of stroke, AMI and colon cancer considered.	Several large RCTs, other prospective studies. Safety and effectiveness not established in this application	Established technology in secondary prevention of stroke and AMI.	**Not adequately validated** in that application **Not supported**
Sex reassignment surgery	Management of gender dysphoria. Other approaches may include counseling, psychotherapeutic approaches	Studies are case series, most reporting on surgical outcomes. More limited data on longer term psychological/ QOL outcomes Thousands of cases	Such surgery in the context of lengthy, detailed preparation including psychological and social support, diagnostic strategies.	**Not adequately validated** **Supported** within framework of international standards and guidelines.

Table 8: Characteristics of technologies considered in some AHFMR assessments (cont'd)

Technology	Nature of disease, application; alternative technologies	Level of evidence, numbers of patients/ clients	Other considerations	Status, Recommendation on support
Technologies that are not experimental, but which required decision on coverage				
Electrical stimulation, fracture healing	Assistance in healing of fractures - for non unions or slow union. Ultrasound stimulation has also been tried.	Some controlled studies, but few rigorous trials. Long-established approach to assist in fracture healing.	Protocols and devices used have varied.	**Not adequately validated** **Supported** in appropriately-selected patients

Notes: Comments on each technology apply to its status at the time of the assessment.

Conclusions on status of each technology not necessarily stated explicitly in original assessments

Appendix C: AHFMR ASSESSMENTS REFERRED TO IN THE REPORT (TABLES 4, 5 AND 6)

Topic	Relevant AHFMR reports
Cord blood transplantation	HTA 18 P Jacobs, D Hailey, N MacLean, *Allogeneic stem cell transplantation,* January 2000 HTA13. M Kwankam, D Hailey, P Jacobs, *Cord blood transplantation*, December 1998 TN7. *Stem cell transplantation*, January 1997 TN4. *Cord blood transplantation,* November 1996
Adult ECMO	TN11. *Extracorporeal life support (ECLS) for children and adults.* July 1997
Bladder ultrasound	HTB1. P Corabian. *Ultrasound measurement of post-void residual urine volume*, August 1996.
Percutaneous ethanol injection therapy	HTB2. P Corabian. *Percutaneous ethanol injection therapy as a treatment for hepatic cancer*, May 1997.
Sex reassignment surgery	TN8. *Vaginoplasty and criteria for M-F sex reassignment surgery.* February 1997 TN6. *Phalloplasty,* December 1996
Electrical stimulation, fractures	TN1. *The use of electrical stimulation to promote healing of fractures*, October 1996
Implantable infusion pump, multiple sclerosis	TN3. *Intrathecal Baclofen using an implantable infusion pump,* November 1996
Hyperbaric oxygen treatment	HTA8. C Mitton, D Hailey. *Hyperbaric oxygen treatment in Alberta*, April 1998.
In vitro fertilization	HTA3. P Corabian. *In vitro fertilization and embryo transfer as a treatment for infertility*, March 1997.
Pallidotomy	HTA2. C Harstall, D Hailey. *Posteroventral pallidotomy in Parkinson's disease*, January 1997.
Pressure measurement devices	HTA1. C Harstall. *Interface pressure measurement systems for management of pressure sores*, September 1996.
Gait analysis	HTA5. J-A Tomie, D Hailey. *Computerized gait analysis in the rehabilitation of children with cerebral palsy and spina bifida*, October 1997.
Lung volume reduction surgery	TN16. *Lung volume reduction surgery (LVRS)*, May 1998
Cryosurgery, prostate cancer	TN15. *Cryosurgery for prostate cancer*, May 1998
Dynamic posturography	HTA7. C Harstall. *Dynamic posturography in the rehabilitation of stroke, brain – injured and amputee patients*, February 1998.
Brachytherapy, prostate cancer	HTA17. F Wills, D Hailey, *Brachytherapy for prostate cancer,* December 1999 TN13. *Brachytherapy for treatment of prostate cancer*, November 1997.

AHFMR assessments referred to in the report (Tables 4, 5 and 6) (cont'd)

Topic	Relevant AHFMR reports
Cabromab pendetide	HTB5. T Howell, D Hailey. *Use of In-111 Capromab Pendetide in detecting metastatic prostate cancer.* November 1999
Radiosurgery	HTA15 W Schneider, D Hailey, *Treatment options for acoustic neuroma,* July 1999 TN17. *Body stereotactic radiosurgery*, May 1998 HTA9. WL. Schneider, D Hailey. *Stereotactic radiosurgery: options for Albertans*, March 1998. TN9. *Radiosurgery in the treatment of malignant melanoma.* February 1997
Vagus nerve stimulation	TN19. Vagus nerve stimulation, November 1998
Telepsychiatry	HTA20. J Simpson, S Doze, D Urness, D Hailey, P Jacobs, *An assessment of routine telepsychiatry services,* November 1999 HTA6. S Doze, J Simpson. *Evaluation of a telepsychiatry pilot project*, November 1997.
Functional Diagnostic Imaging	HTA16. D Cowley, P Corabian, D Hailey, *Functional diagnostic imaging technologies in the assessment of myocardial viability,* October 1999 HTA10. P Corabian, D Hailey. *Functional diagnostic imaging in epilepsy,* August 1998.
Tests for vaginitis	HTA12. C Harstall, P Corabian. *Diagnostic tests for vaginosis/ vaginitis*, October 1998
Air plethysmography	TN12. *Air plethysmography for venous evaluation.* November 1997
Laser ophthalmology	TN5. *Scanning laser ophthalmoscope for diagnosis and monitoring of glaucoma*, December 1996
Ultrasonic bone density measurement	HTA11. J Homik, D Hailey. *Quantitative ultrasound for bone density measurement,* September 1998
Lasers for wound healing	HTA19. W Schneider, D Hailey, *Low level laser therapy for wound healing,* October 1999
Aspirin in primary prevention, AMI etc.	HTB3. D Hailey, C Harstall. *Aspirin in the primary prevention of cardiovascular disease and colon cancer,* November 1997

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